AMENDMENTS TO THE CLAIMS

Please cancel claim 12 without prejudice. This listing of claims will replace all prior versions and listings of claims in the application:

Listing of Claims:

1. **(Original)** A chimeric nuclease, comprising: (i) a DNA binding domain; (ii) a cleavage domain; and (iii) a nuclear localization signal.

2. **(Original)** The chimeric nuclease of claim 1, wherein the DNA binding domain binds to a recognition sequence comprising at least 6 designated nucleotides.

3. **(Original)** The chimeric nuclease of claim 1, wherein the DNA binding domain comprises at least one zinc finger domain.

4. **(Original)** The chimeric nuclease of claim 1, wherein the DNA binding domain comprises three or more zinc finger domains.

5. **(Original)** The chimeric nuclease of claim 1, wherein the cleavage domain comprises a cleavage domain of a type IIs restriction endonuclease.

6. **(Original)** The chimeric nuclease of claim 1, wherein the cleavage domain comprises a cleavage domain of a FokI restriction endonuclease.

7. **(Original)** The chimeric nuclease of claim 1, wherein the DNA binding domain comprises three zinc finger domains and binds to a recognition sequence comprising 9 designated nucleotides, and wherein the cleavage domain is a cleavage domain of a FokI restriction endonuclease.

8. **(Currently amended)** A chimeric nuclease, comprising:
(a) a nuclear localization signal;
(~~a~~ b) a cleavage domain; and
(~~b~~ c) a DNA binding domain comprising at least three zinc fingers,
wherein the DNA binding domain binds to a recognition sequence that occurs at a position in a mammalian genome within ~~at least~~ 500 base pairs of an allele that is known

to contribute[[s]] to a genetic disorder, and wherein the recognition sequence comprises at least 9 nucleotides.

9. **(Currently amended)** A complex comprising a first chimeric nuclease and a second chimeric nuclease, wherein the first chimeric nuclease comprises a nuclear localization signal, a cleavage domain and a DNA binding domain, and wherein the second chimeric nuclease comprises a nuclear localization signal, a cleavage domain and a DNA binding domain.

10. **(Original)** The complex of claim 9, wherein the first chimeric nuclease comprises a DNA binding domain that comprises at least three zinc finger domains and that recognizes a sequence comprising at least 9 designated nucleotides.

11. **(Original)** The complex of claim 10, wherein the second chimeric nuclease comprises a DNA binding domain that comprises at least three zinc finger domains and that recognizes a sequence comprising at least 9 designated nucleotides.

12. **(Canceled)**

13. **(Original)** A nucleic acid encoding a chimeric nuclease, wherein the chimeric nuclease comprises: (i) a DNA binding domain; (ii) a cleavage domain; and (iii) a nuclear localization signal (NLS).

14-17. **(Canceled)**

18. **(Currently amended)** A nucleic acid encoding a chimeric nuclease, the chimeric nuclease comprising:
(a) a nuclear localization signal;
(~~a~~ b) a cleavage domain; and
(~~b~~ c) a DNA binding domain comprising at least three zinc fingers,
wherein the DNA binding domain binds to a recognition sequence that occurs at a position in a mammalian genome within ~~at least~~ 500 base pairs of an allele that is known to contribute[[s]] to a genetic disorder, and wherein the recognition sequence comprises at least 9 nucleotides.

19. **(Canceled)**

20. **(Currently amended)** A vector comprising
(a) a nucleic acid encoding a first chimeric nuclease; and
(b) a nucleic acid encoding a second chimeric nuclease,
wherein the second chimeric nuclease forms a heterodimer with said first chimeric nuclease, wherein the first chimeric nuclease and/or the second chimeric nuclease comprises a nuclear localization signal.

21. **(Currently amended)** A vector comprising:
(1) a nucleic acid encoding a chimeric nuclease that comprises: (i) a DNA binding domain; ~~and~~ (ii) a cleavage domain; and (iii) a nuclear localization signal; and
(2) a nucleic acid comprising a repair substrate that comprises: (i) a nucleic acid sequence that is substantially identical to a region flanking a target sequence in chromosomal DNA; and (ii) a nucleic acid sequence which replaces the target sequence upon recombination between the repair substrate and the target sequence.

22-27. **(Canceled)**

28. **(Currently amended)** A mammalian cell comprising: (a) a chimeric nuclease; and (b) a repair substrate, wherein the chimeric nuclease comprises:
(i) a nuclear localization signal;
(ii) a DNA binding domain; and
(iii) a cleavage domain,
and wherein the repair substrate comprises:
(i) a nucleic acid sequence that is substantially identical to a region flanking a target sequence in chromosomal DNA; and
(ii) a nucleic acid sequence which replaces the target sequence upon recombination between the repair substrate and the target sequence.

29-39. **(Canceled)**

40. **(Currently amended)** A mammalian cell comprising a nucleic acid encoding a chimeric nuclease and a nucleic acid comprising a repair substrate, wherein the chimeric nuclease comprises:
(i) a nuclear localization signal;
(ii) a DNA binding domain; and

(iii) a cleavage domain,
and wherein the repair substrate comprises:
(i) a nucleic acid sequence that is substantially identical to a region flanking a target sequence in chromosomal DNA; and
(ii) a nucleic acid sequence which replaces the target sequence upon recombination between the repair substrate and the target sequence.

41-42. **(Canceled)**

43. **(Original)** A method of changing a target sequence in genomic DNA of a mammalian cell, comprising:
(a) introducing a chimeric nuclease, or nucleic acid encoding the chimeric nucleic acid, into the cell, wherein said chimeric nuclease comprises: (i) a DNA binding domain; and (ii) a cleavage domain; and
(b) introducing a repair substrate into the cell, wherein said repair substrate comprises: (i) a nucleic acid sequence that is substantially identical to a region surrounding the target sequence; and (ii) a nucleic acid sequence which changes the target sequence upon recombination between the repair substrate and the target sequence,
whereby the target sequence is changed by the repair substrate upon recombination.

44-97. **(Canceled)**

98. **(Previously presented)** The vector of claim 21, wherein the chimeric nuclease further comprises a nuclear localization signal.

99. **(Previously presented)** The vector of claim 21, wherein the nucleic acid encoding the chimeric nuclease is operably linked to a promoter.

100. **(Previously presented)** The vector of claim 99, wherein the promoter is an inducible promoter.

101. **(Previously presented)** The vector of claim 99, wherein the vector is a viral vector.

102. **(Previously presented)** The vector of claim 21, further comprising a nucleic acid encoding a second chimeric nuclease, wherein the second chimeric nuclease forms a heterodimer with said chimeric nuclease.

103. **(Previously presented)** The cell of claim 28, wherein the chimeric nuclease is encoded by a nucleic acid that is operably linked to a promoter in a vector.

104. **(Previously presented)** The cell of claim 103, wherein the promoter is an inducible promoter.

105. **(Previously presented)** The cell of claim 28, wherein the chimeric nuclease further comprises a nuclear localization signal.

106. **(Previously presented)** The cell of claim 28, wherein the DNA binding domain of the chimeric nuclease comprises a zinc finger domain.

107. **(Previously presented)** The cell of claim 28, wherein the cleavage domain comprises a cleavage domain of a type IIs restriction endonuclease.

108. **(Previously presented)** The cell of claim 107, wherein the cleavage domain comprises a FokI cleavage domain.

109. **(Previously presented)** The method of claim 43, wherein the target sequence contains an allele that contributes to a disease that is repaired by the repair substrate.

110. **(Previously presented)** The method of claim 43, wherein the target sequence is situated in a gene that is attenuated or inactivated by the repair substrate.

111. **(Previously presented)** The method of claim 43, wherein the target sequence is replaced by a heterologous sequence in the repair substrate.

112. **(Previously presented)** The method of claim 111, wherein the heterologous sequence comprises the coding sequence of a transgene.

113. **(Previously presented)** The method of claim 111, wherein the target sequence is selected such that the coding sequence of a transgene is inserted at a transcriptionally active site.

114. **(Previously presented)** The method of claim 43, wherein introducing the chimeric nuclease into the cell comprises introducing a nucleic acid encoding the chimeric nuclease into the cell, whereby the chimeric nuclease is produced in cell.

115. **(Previously presented)** The method of claim 114, wherein the nucleic acid encoding the chimeric nuclease and the repair substrate are present in a single vector introduced into the cell.

116. **(Previously presented)** The method of claim 114, wherein the nucleic acid encoding the chimeric nuclease is operably linked to a promoter in a vector.

117. **(Previously presented)** The method of claim 116, wherein the promoter is an inducible promoter.

118. **(Previously presented)** The method of claim 43, wherein the chimeric nuclease further comprises a nuclear localization signal.

119. **(Previously presented)** The method of claim 43, wherein the DNA binding domain of the chimeric nuclease comprises a zinc finger binding domain.

120. **(Previously presented)** The method of claim 43, wherein the cleavage domain comprises a cleavage domain of a restriction endonuclease.

121. **(Previously presented)** The method of claim 120, wherein the cleavage domain comprises a FokI cleavage domain.

122. **(Previously presented)** The method of claim 43, wherein the chimeric nuclease forms a heterodimer of two different chimeric nucleases.

123. **(Previously presented)** The method of claim 43, wherein the target sequence includes an allele that participates in the causation of a disease.